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(51) International Patent Classification <sup>6</sup> : <b>A61K 31/47</b>		<b>A3</b>	(11) International Publication Number: <b>WO 99/00117</b> (43) International Publication Date: <b>7 January 1999 (07.01.99)</b>
(21) International Application Number: <b>PCT/US98/13387</b> (22) International Filing Date: <b>26 June 1998 (26.06.98)</b> (30) Priority Data: <b>08/883,656</b> <b>27 June 1997 (27.06.97)</b> <b>US</b> (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application <b>US</b> <b>08/883,656 (CIP)</b> <b>Filed on</b> <b>27 June 1997 (27.06.97)</b> (71) Applicant (for all designated States except US): <b>ONTOGENY, INC. [US/US]; 45 Moulton Street, Cambridge, MA 02138 (US).</b> (72) Inventor; and (75) Inventor/Applicant (for US only): <b>MAHANTHAPPA, Nagesh, K. [US/US]; 240 Norfolk Street, Cambridge, MA 02139 (US).</b> (74) Agents: <b>VINCENT, Matthew, P. et al.; Foley, Hoag &amp; Eliot LLP, One Post Office Square, Boston, MA 02109 (US).</b>			(81) Designated States: <b>AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</b> <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: <b>1 April 1999 (01.04.99)</b>
(54) Title: <b>NEUROPROTECTIVE METHODS AND REAGENTS</b>			
(57) Abstract <p>One aspect of the present application relates to a method for limiting damage to neuronal cells by ischemic or epoxic conditions, e.g., such as may be manifest by a reduction in brain infarct volume, by administering to an individual a hedgehog therapeutic or ptc therapeutic in an amount effective for reducing cerebral infarct volume.</p>			

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 98/13387

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61K31/47

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 519 035 A (MAIESE KENNETH ET AL) 21 May 1996  see abstract see column 2, line 20-34; claims 1-5; examples 1,2  ---	1-12, 16-19, 21-28, 30-38
X	SATOH ET AL.: "Neuroprotective properties of a protein kinase inhibitor against Ischemia-induced neuronal damage in rats and gerbils" BRITISH JOURNAL OF PHARMACOLOGY, vol. 118, no. 7, 1996, pages 1592-1596, XP002092077 see abstract  ---	1-12, 16-19, 22-28, 30-38
-/--		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
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- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

3 February 1999

Date of mailing of the international search report

18/02/1999

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/13387

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>MAIESE ET AL.: "Protein Kinases Modulate the Sensitivity of Hippocampal Neurons to Nitric Oxide Toxicity and Anoxia" JOURNAL OF NEUROSCIENCE RESEARCH, vol. 36, no. 1, 1993, pages 77-87, XP002092078 see abstract see page 79, column 1, paragraph 1 - page 81, column 2, paragraph 2; figure 1 see page 83, column 2, paragraph 2 - page 84, column 1, paragraph 3 ---</p>	<p>1-12, 16-28, 30-38</p>
X	<p>PHILLIS ET AL.: "Mechanism of glutamate and aspartate release in the ischemic rat cerebral cortex" BRAIN RESEARCH, vol. 730, no. 1-2, 1996, pages 150-164, XP002092079 see abstract; figure 7; tables 2,3 ---</p>	<p>1-12, 16-28, 30-38</p>
X	<p>EP 0 187 371 A (ASAHI CHEMICAL IND ;HIDAKA HIROYOSHI (JP)) 16 July 1986  see abstract see page 2, line 1-10; example 4 see page 8, line 6 - page 14, line 4 ---</p>	<p>1-12, 16-19, 22-28, 30-38</p>
P,X	<p>WO 98 12326 A (CHUANG PAO TIEN ;HARVARD COLLEGE (US); MCMAHON ANDREW P (US)) 26 March 1998 see page 3, line 15 - page 9, line 10; claim 13 -----</p>	<p>1-14,40</p>

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/ 13387

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-34, 40  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 1-34, 40  
are directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☒ Claims Nos.: -  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:  
See FURTHER INFORMATION SHEET PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

In view of the large number of compounds, which are defined by the general definition(s)/formulae used in claims 1-20, 22-40, the search had to be restricted for economic reasons. The search was limited to the compounds for which pharmacological data was given and/or the compounds mentioned in the claims, and to the general idea underlying the application. (See Guidelines, chapter III, paragraph 2.3).

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/13387

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5519035	A	21-05-1996	NONE	
EP 0187371	A	16-07-1986	JP 1795364 C	28-10-1993
			JP 5003851 B	18-01-1993
			JP 61227581 A	09-10-1986
			JP 1789975 C	29-09-1993
			JP 4081986 B	25-12-1992
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			US 4678783 A	07-07-1987
WO 9812326	A	26-03-1998	AU 4489297 A	14-04-1998